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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,111	03/12/2001	Nongnuch Inpanbutr	06204-00102	8670

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EXAMINER	
BAHAR, MOJDEH	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/804,111	INPANBUTR, NONGNUCH	
	Examiner	Art Unit	
	Mojdeh Bahar	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 18-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 18-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Action

Applicant's response to the restriction requirement and amendment submitted December 21, 2001 (Paper No. 7) is acknowledged.

Applicant's election therein of the invention of Group I, claims 1-12 in Paper No. 7 submitted December 21, 2001 is acknowledged.

Election was made **without** traverse in Paper No. 7.

Claims 1-12 and 18-25 are examined on the merits herein.

Claim Objections

Claims 2, 4, 5, 18, 19 and 24 are objected to because of the following informalities: the employment of parenthetical expressions "(analog V)", "(EB 1089)", "(DHEA)", "(hydroxydaunorubicin)", "(oncovin)" and "(buffer)" is considered informal. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 and 18-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some types of cancer, does not reasonably provide enablement for all cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to make and/or use the invention, and thereby failing to provide an enabling disclosure.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that defines what types of "cancer" can be treated with the instant method. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these types of "cancer" without undue experimentation. In the instant case, only a limited number of cancer (SCC288 in the specification) examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of cancers against which the instant method is useful.

The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity in every type of cancer. The instant claims read on all types of cancer necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-12 and 18-25 are rejected under 35 USC section 101 because the claimed invention, setting forth an incredible utility, treatment of all cancer, lacks patentable utility.

It is well settled patent law that all inventions seeking patent protection under United States Codes must be useful. The profered claims 1-12 and 18-25 read on treating all cancers, thereby failing to set forth a credible utility. The skilled artisan would view cancer as a group of maladies not treatable with one medicament or therapeutic regimen. Claims directed to treating all cancer would be seen as an incredible utility.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5, 7-12 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boggolini et al. (USPN 5,087,619) and Yu et al (PMID 7756673).

Boggiolini et al. (USPN 5,087,619) teaches a method of treating neoplastic diseases in a warm-blooded animal comprising administering an effective amount of a vitamin D3 analogue (e.g., 1,25 $(OH)_2$ D3 and 1,2-16 delta-23-yne-D3), see for example tables III and IV, claim 20 and abstract. Boggiolini et al. (USPN 5,087,619) also teaches vitamin D3 analogues in oral dosage forms such as capsules, see col. 21, lines 37-40. Pharmaceutically acceptable carrier materials may be incorporated in capsules, such as starch, magnesium stearate, lactose, peppermint oil (flavoring agent), see in particular col. 21, line 37 to col. 22, line 27. Boggiolini et al. (USPN 5,087,619) also teaches that the dosage for the vitamin D3 analogues is 0.1 to 10 microgram per day, see col. 11, lines 16-24.

Yu et al. teaches that EB1089 is known to inhibit cell proliferation and is useful against neoplastic diseases, see abstract.

Boggolini et al. (USPN 5,087,619) and Yu et al (PMID 7756673) taken together do not teach the doses claimed herein in terms of nmol/Kg, neither do they teach all the pharmaceutical excipients and auxillaries claimed herein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ/express the amounts of active in terms of nmol/Kg. It would have also been obvious to employ any known pharmaceutical excipients and auxillaries in the composition employed in the instant method.

One of ordinary skill in the art would have been motivated to employ/express the amounts of active in terms of nmol/Kg because optimization of amounts is within the skill of the artisan and is therefore obvious. Similarly the employment of any known pharmaceutical excipient and/or auxillaries with a known active is within the skill of the artisan and therefore obvious.

Claims 6 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boggolini et al. (USPN 5,087,619) and Yu et al (PMID 7756673) in view of Katzung.

Boggiolini et al. (USPN 5,087,619) teaches a method of treating neoplastic diseases in a warm-blooded animal comprising administering an effective amount of a vitamin D3 analogue (e.g., 1,25 $(OH)_2$ D3 and 1,2-16 delta-23-yne-D3), see for example tables III and IV, claim 20 and abstract. Boggiolini et al. (USPN 5,087,619) also teaches vitamin D3 analogues in oral dosage forms such as capsules, see col. 21, lines 37-40. Pharmaceutically acceptable carrier materials may be incorporated in capsules, such as starch, magnesium stearate, lactose, peppermint oil (flavoring agent), see in particular col. 21, line 37 to col. 22, line 27. Boggiolini et al. (USPN 5,087,619) also teaches that the dosage for the vitamin D3 analogues is 0.1 to 10 microgram per day, see col. 11, lines 16-24.

Yu et al. teaches that EB1089 is known to inhibit cell proliferation and is useful against neoplastic diseases, see abstract.

Boggiolini et al. (USPN 5,087,619) and Yu et al (PMID 7756673) taken together do not teach the inclusion of a second active (i.e., bone agent, cytotoxic agent or anti inflammatory agent) in a composition employed in a method of treating cancer.

Katzung teaches that hypercalcemia is a consequence of hypervitaminosis D. Katzung further teaches that bisphosphonates, calcitonin are employed in treating hypercalcemia, see pages 661-663. Katzung also teaches the employment of estrogen inhibitors, mitomycin, vincristine, doxorubicin, fluorouracil for treating different cancers, see page 838 and 841. Katzung further teaches cisplatin, melphalan, and methoxorate as anti-cancer agents, see pages 830-832. Both Salicylates and Naproxen are known NSAIDS (known for their anti-inflammatory and analgesic properties), 537-538.

Harman et al. teaches that pain is commonly associated with cancer, see page 539.

It would have been obvious to one of ordinary skill at the time the invention at the time the invention was made to employ a second active (i.e., bone agent, cytotoxic agent or anti inflammatory agent) in a composition employed in a method of treating cancer.

One of ordinary skill in the art would have been motivated to employ bisphosphonates and calcitonin in a method of treating cancer employing a vitamin D3 analogue/derivative because they are known to be employed in methods of preventing and/or treating hypercalcemia associated with vitamin D administration. One of ordinary skill in the art would have been motivated to employ Salicylates and Naproxen, known NSAIDS, known for their anti-inflammatory and analgesic properties, in a method of treating cancer because pain is known to be associated with cancer.

One of ordinary skill in the art would have been motivated to employ estrogen inhibitors, mitomycin, vincristine, doxorubicin, fluorouracil cisplatin, melphalan, and methoxorate along with Vitamin D derivatives in a method of treating cancer. Estrogen inhibitors, mitomycin, vincristine, doxorubicin, fluorouracil cisplatin, melphalan, and methoxorate are known to be employed in methods of treating cancer. Combining two agents which are known to be useful to treat cancer individually into a single composition useful for the very same purpose (i.e. treating cancer) is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 from 8:30 a.m. to 6:30 p.m. Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
February 26, 2002

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